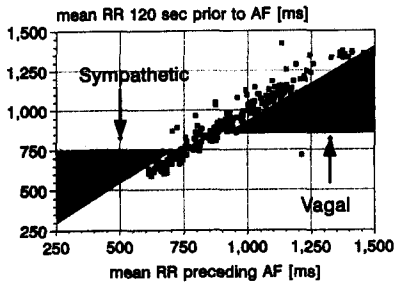
illustrate, respectively, where vagal and sympathetic onset episodes would be expected to be found.



Conclusions: No heart rate change suggestive of high autonomic tone is demonstrable in an unselected population with symptomatic PAF.

743 Vascular Biology: Nitric Oxide

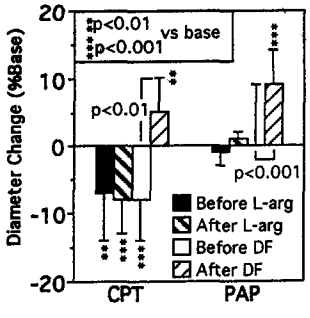
Tuesday, March 18, 1997, 10:30 a.m.–Noon
Anaheim Convention Center, Room B1

10:30

743-1 Coronary Artery Responses to Cold Pressor Test and to Flow Increase are Improved by Desferrioxamine but not L-Arginine in Diabetic Patients With Normal Coronary Arteries

A. Nitenberg, S. Ledoux, P. Valensi, J.-R. Attali. *INSERM U.426, Hôpital Louis Mourier, Colombes, France*

We have previously demonstrated that acetylcholine produces coronary constriction in diabetic patients suggesting that EDRF-mediated dilation is impaired. In order to elucidate the mechanism of this abnormal response, flow-dependent (FD) and cold pressor test (CPT)-induced coronary artery (CA) responses were evaluated in 2 groups of normotensive diabetic patients with angiographically normal coronary arteries and normal cholesterol. In group 1 (n = 7), measures were made before and after i.v. L-arginine (L-arg), and before and after i.v. desferrioxamine (DF) in group 2 (n = 8). Dimensions of proximal left anterior descending (LADp) CA were determined by quantitative angiography at base, during CPT, and after 10 mg papaverine (PAP) into the distal LAD. Results show that before administration of L-arg or DF, LADp diameters were reduced during CPT and did not change after PAP. Administration of L-arg did not modify the response to CPT and PAP. Conversely, LADp dilated after administration of DF in response to CPT and PAP. Isosorbide dinitrate produced similar dilation in the 2 groups (+18 ± 5% and +14 ± 4%, respectively).



Conclusions: 1) FD and CPT-induced CA responses are impaired in diabetic patients; 2) responses are not modified by L-arg suggesting that a deficit in substrate for NO synthesis is not involved; 3) DF improves the response suggesting that inactivation of NO by superoxyde radicals might be responsible of the impairment of coronary vasomotion in diabetic patients.

10:45

743-2 Converting Enzyme Inhibition Improves Endothelial Dysfunction in Humans by Increasing Nitric Oxide Activity

A. Prasad, S. Husain, R. Mincemoyer, L. Hathaway, A.A. Quyyumi. *National Institutes of Health, Bethesda, MD, USA*

Angiotensin converting enzyme inhibitors (ACEI) have vasculoprotective effects. We hypothesized that this is due to their ability to reduce bradykinin (BK) degradation and thus increase nitric oxide activity. In the femoral circulation of 45 pts, 41 of whom had atherosclerosis or its risk factors, we studied endothelium-dependent vasodilation with BK (250 ng/min) and acetylcholine (ACh, 300 μg/min), and endothelium-independent vasodilation with sodium nitroprusside (SNP, 40 μg/min) before and after enalaprilat (EN, 20 μg/min). In 16 pts, we repeated the infusions in the presence of L-N^G monomethyl arginine (L-NMMA, 64 μmol/min), an inhibitor of nitric oxide synthase. Femoral artery flow velocity was measured using a Doppler flow wire and the resistance index (RI = mmHg·cm^{-1}·sec) calculated as mean arterial pressure ÷ flow velocity. EN did not alter resting RI (5.8 ± 1.8, mean ± SD) but enhanced BK mediated dilation (2.7 ± 1.0 to 2.0 ± 0.7 RI, $p < 0.001$). The potentiation of ACh mediated dilation with EN was inversely proportional to the baseline ACh response ($r = -0.5$, $p < 0.005$). EN did not potentiate SNP mediated vasodilation. L-NMMA inhibited the effect of BK ($p < 0.07$) and ACh ($p = 0.02$), but not SNP ($p = 0.7$). Furthermore, in the presence of L-NMMA, EN did not potentiate BK (3.1 ± 1.1 to 3.6 ± 1.4 RI) and ACh (5.3 ± 2.6 to 5.4 ± 3.1 RI) responses. These findings suggest that ACEI selectively improve endothelium-dependent vascular function in pts, particularly those with endothelial dysfunction. Increased nitric oxide activity with ACEI is in part responsible for this beneficial effect.

11:00

743-3 Racial Differences in Nitric Oxide-Mediated Response to Mental Stress in the Forearm Circulation

C. Cardillo, C.M. Kilcoyne, A.A. Quyyumi, R.O. Cannon, III, J.A. Panza. *NHLBI, Bethesda, MD*

An abnormal hemodynamic response to stressful stimuli has been proposed as a mechanism involved in the higher prevalence of hypertension in blacks. Given the important role of nitric oxide (NO) in the modulation of the cardiovascular adaptation to a variety of stimuli, we postulated that racial differences may exist in the vascular release of NO in response to mental stress. To test this hypothesis, we compared the effects of mental arithmetic test (MAT; repeated subtraction of 7 from a 3-digit number for 3 min) on forearm vascular dynamics (plethysmography) in 14 white (W) (7 men; age 49 ± 9 years) and 13 black (B) (6 men; age 43 ± 8 years) normal subjects during intraarterial infusion of saline (S) or L-NMMA (4 μmol/min), a blocker of NO synthesis. The effect of L-NMMA on endothelium-independent relaxation was studied during intraarterial infusion of sodium nitroprusside (SNP; 0.8–3.2 μg/min). During S, the increase in forearm blood flow (FBF) induced by MAT was significantly higher in W than in B (109 ± 73% vs 58 ± 26%; $P < 0.01$). L-NMMA significantly reduced MAT-induced increase in FBF in W (to 54 ± 42%; $P = 0.004$ vs S), but not in B (to 40 ± 34%; $P = 0.14$ vs S). The vasodilator effect of SNP was also lower in B than in W (maximum flow: 6.9 ± 2 vs 11.6 ± 3.5 mL/min/dL; $P = 0.001$), indicating an impaired smooth muscle dilator response to NO in B. L-NMMA infusion did not modify the vasodilator effect of SNP either in W (10.9 ± 3.5 mL/min/dL; $P = 0.4$ vs S) or in B (7.2 ± 2.1 mL/min/dL; $P = 0.6$ vs S). In conclusion, B have a reduced NO vasodilating activity during mental stress, that seems to be related to an impaired sensitivity of smooth muscle cells to the effect of NO.

11:15

743-4 Oral Chronic L-arginine Administration Improves Coronary Endothelial Function In Humans

A. Lerman, L. McKinley, S.T. Higano, D.R. Holmes. *Mayo Clinic, Rochester, MN, USA*

The endothelium regulates coronary vascular tone by releasing endothelium-derived nitric oxide. Acute administration of L-arginine (ARG), the substrate for endothelium derived nitric oxide, in humans attenuated coronary endothelial dysfunction in response to the endothelial-derived vasodilator acetylcholine. This study was designed to test the hypothesis that chronic oral administration of ARG improves endothelial function in patients with documented coronary endothelial dysfunction associated with no significant coronary artery disease. Thus, coronary angiography with graded selective infusions of acetylcholine (10^{-6} to 10^{-4} M) into the left anterior descending artery (LAD), was performed in 18 patients at baseline and at 6 months following